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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,742	01/22/2004	Yuhpyng L. Chen	PC9574C	5579

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EXAMINER

HABTE, KAHSA Y

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 02/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/762,742	<b>Applicant(s)</b> CHEN, YUHPYNG L.	
	<b>Examiner</b> Kahsay Habte	<b>Art Unit</b> 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 24 January 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 9-11, 18, 19, 22 and 23 is/are pending in the application.
- 4a) Of the above claim(s) 10, 22 and 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 18 is/are rejected.
- 7) ☒ Claim(s) 9, 11 and 19 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

1. Claims 9-11, 18-19 and 22-23 are pending in this application.

### ***Response to Amendment***

2. Applicant's amendment filed 1/24/2006 in response to the previous Office Action (11/01/2005) is acknowledged. Rejections of claims 9, 11, 19 and 23 under 35 U.S.C. § 112, second paragraph (items 8a-8b) and the obviousness-type patenting (items 6-7) have been obviated.

3. Since the condition for rejoinder is met, claim 18 (method claim) that was withdrawn from prosecution is now rejoined. The restriction requirement between Group I and V is withdrawn.

### ***Claim objection***

4. Claims 9, 11 and 19 are objected to because claim 9 is drawn to multiple inventions for reasons set forth in the restriction requirement. The claims are examined only to the extent that they read on the elected invention. Cancellation of the non-elected subject matter is recommended in response to this Office Action. Note that Group I is drawn to (Pyrazolo[1,5-a]pyrimidines where A and E = C. Applicants have to delete the non-elected subject matter from claim 9, this can be done by deleting the definition of E = S, O or NR<sup>8</sup>.

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Claim 23 is withdrawn from prosecution, because the species left in claim 23 are drawn to non-elected inventions. Note that applicants deleted all the (Pyrazolo[1,5-a]pyrimidines species to overcome double-patenting rejection. It is recommended that applicants delete claims 10, 22 and 23 that are drawn to non-elected inventions.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In claim 18, it is recited a method of treating or preventing a disorder or condition, the treatment or prevention of which can be affected or facilitated by inhibiting CRH binding protein in a mammal, comprising administering to said mammal a CRH binding protein inhibiting amount of a compound, but the specification is not enabled for such a scope.

A number of factors are relevant to whether undue experimentation would be required to practice the claimed invention, including "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior

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art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.” In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The instant claims recite “A method of treating or preventing a disorder or condition, the treatment or prevention of which can be affected or facilitated by inhibiting CRH binding protein in a mammal, comprising administering to said mammal a CRH binding protein inhibiting amount of a compound” and the specification on pages 1-2 provides that CRH (CRF) antagonists are effective in the treatment of myriad disorders such as inflammatory disorders, eating disorders, mood disorders, stress-related illnesses, chronic fatigue syndrome,, panic disorder, phobias, headache, gastrointestinal disorders, pain, asthma, psoriasis, allergies, sleep disorders, neurodegenerative diseases such as Alzheimer’s disease and senile dementia, cancer, etc. wherein there is insufficient description in the specification regarding the treatment of said diseases. The nature of the diseases that applicants intend to treat or prevent is different one from the other. Please see below.

The claim sets forth the treatment of cancer generally. However, there never has been a compound capable of treating cancer generally. There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a “silver bullet” is contrary to our present understanding in oncology. Even the most broadly effective antitumor agents are only effective against a small

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fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

Enablement for the scope of "inflammation" generally is not present. For a compound or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process which can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, assorted leukotrienes and cytokines, and many, many others. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally.

Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or

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continuing injury. The principal features are dilatation and leaking of vessels, and recruitment of circulating neutrophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. They are clusters of macrophages which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters.

Otitis media is an inflammation of the lining of the middle ear and is commonly caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*. Cystitis is an inflammation of the bladder, usually caused by bacteria. Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasolacrimal duct and is caused by staphylococci or streptococci. Preseptal cellulitis is inflammation of the tissues around the eye, and Orbital cellulitis is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics.

Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases. The above list is by no means complete, but demonstrates the

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extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to any agent to be able to treat inflammation generally.

A method of treating gastrointestinal disease (GI) has been claimed, but there is no enablement in the specification for such a scope. Gastrointestinal disease includes diseases of the esophagus (e.g. Achalasia, gastroesophageal reflux disease), diseases of the stomach and duodenum (e.g. gastritis) and the rest of the digestive system, which includes the GI itself plus three digestive organs (spleen, pancreas and liver). It also includes inflammatory bowel disease, infectious disease of the intestines, malabsorption, surgical non-neoplastic disease of the GI tract, tumors of the GI tract, Barrett's Oesophagus, Chronic Hepatitis, Cirrhosis, Coeliac Disease, Colorectal Cancer, Collagenous colitis, Colorectal Polyps, Crohn's Disease, Diverticulosis and Diverticulitis, Fatty Liver, Gastric Cancer, Gallstones, Haemochromatosis, Helicobacter pylori infection, Irritable Bowel Syndrome, Liver Failure and Liver Transplantation, Lymphocytic colitis, Microscopic colitis, Oesophageal Cancer, Pancreatitis, Peptic Ulcers, Primary Biliary Cirrhosis (PBC), Reflux Oesophagitis, Ulcerative Colitis, Viral Hepatitis, etc.

As shown by Thomas A. Godwin (GASTROINTESTINAL DISEASES, <[http://edcenter.med.cornell.edu/CUMC\\_PathNotes/Gastrointestinal/Gastrointestinal.html](http://edcenter.med.cornell.edu/CUMC_PathNotes/Gastrointestinal/Gastrointestinal.html)>, 51 pages), the nature of the gastrointestinal disease and gastrointestinal conditions are extremely different one from the other. To this day, no one was able to treat



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gastrointestinal disease and gastrointestinal conditions with a single drug. Thus, the enablement rejection is proper.

The scope of the claims is not adequately enabled. There is no working example or test procedure to find the  $K_i$  values of the compounds with respect to inhibition of CRH binding. There is nothing in the disclosure regarding how inhibition of CRH binding correlates to the treatment of all the disorders embraced the instant claims. The disorders encompassed by the instant claims include a sleep disorder, cancer, Alzheimer's disease, some of which have been proven to be extremely difficult to treat. There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 1 51 USPQ 724 regarding sufficiency of disclosure for a Markush group.

Thus, factors such as 'sufficient working examples', 'the level of skill in the art' and 'predictability', etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

In regard to the method of prevention, to this day no one was able to accomplish in preventing healthy people from getting all the diseases disclosed in pages 1-2 of the

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specification in the first place. It is recommended that applicants delete claim 18 to overcome this rejection.

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 18, it is recited a method of treating or preventing a disorder or condition, the treatment or prevention of which can be affected or facilitated by inhibiting CRH binding protein in a mammal. The scope of claim 18 is unknown. Which diseases are these? Determining whether a given disease responds or does not respond to such mediator will surely involve undue experimentation. Suppose that a given inhibitor X when administered to a patient with Disease D does not obtain a response. Does one then conclude that Disease D does not fall within this claim? Keep in mind that:

A. It may be that the next patient will respond. It is quite common for pharmaceuticals to work only with some people, not all. Thus, how many need to be tested?

B. It may be that the wrong dosage or dosage regimen was employed. It is quite common for pharmaceuticals to work at one dosage, but not at another which is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? Thus, how many dosages and dosage regimens must be tried before one is certain that this pharmaceutical won't affect Disease D?

C. It may be that X simply isn't potent enough for Disease D, but that another inhibitor Y is potent enough, so that D really does fall within the claim. Thus, how many different mediators must be tried before one concludes that D doesn't fall within the claim?

D. Conversely, if D responds to Y but not to X, can one really conclude that D falls within the claim? It may be that the X result is giving the accurate answer, and that the success of Y arises from some other unknown property which Y is capable of. Thus, when mixed results are obtained, how many more pharmaceuticals need be tested?

E. Finally, suppose that X really will work, but only when combined with Z. There are for example, agents in the antiviral and anticancer technology which are not themselves effective, but the disease will respond when the agents are combined with something else.

F. In addition, literally speaking, any disorder can be treated with any drug, although the treatment might not be successful. Assuming that "successful treatment"

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is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000?

As a result, determining the true scope of the claim will involve extensive and potentially open-ended research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

### ***Conclusion***

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay Habte, Ph. D. whose telephone number is (571) 272-0667. The examiner can normally be reached on M-F (9.00AM- 5:30PM).

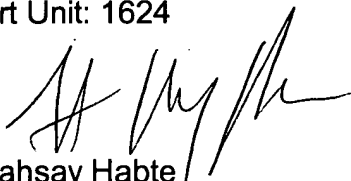
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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A handwritten signature in black ink, appearing to read 'Kahsay Habte', written in a cursive style.

Kahsay Habte  
Primary Examiner  
Art Unit 1624

KH  
February 15, 2006